



General

Guideline Title

ACR Appropriateness Criteria® local-regional recurrence (LRR) and salvage surgery—breast cancer.

Bibliographic Source(s)

Halyard MY, Haffty BG, Harris EE, Bailey L, Bellon JR, Freedman GM, Goyal S, Horst KC, Moran MS, Park CC, Suh WW, Toppmeyer D, Expert Panel on Radiation Oncology—Breast. ACR Appropriateness Criteria® local-regional recurrence (LRR) and salvage surgery—breast cancer. [online publication]. Reston (VA): American College of Radiology (ACR); 2013. 12 p. [51 references]

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Halyard MY, Wasif N, Haffty BG, Harris EE, Arthur DW, Bailey L, Bellon JR, Carey L, Goyal S, Horst KC, MacDonald SM, Moran MS, Expert Panel on Radiation Oncology-Breast. ACR Appropriateness Criteria® local-regional recurrence (LR) and salvage surgery -- breast cancer. [online publication]. Reston (VA): American College of Radiology (ACR); 2010. 8 p.

Recommendations

Major Recommendations

ACR Appropriateness Criteria®

Clinical Condition: Local-Regional Recurrence (LRR) and Salvage Surgery—Breast Cancer

Variant 1: 52-year-old woman, 0.5-cm LRR in breast, 15 years after BCT with lumpectomy and axillary node dissection + RT for T1bN0 lesion. Biopsy showed invasive ductal carcinoma. ER/PR (+). HER-2 negative/nonamplified. EOD workup negative.

Treatment	Rating	Comments
Principles of Treatment		
Hormone therapy	6	No trial data exists to support in this setting. One could infer possible benefit from data provided by the SAKK trial, which demonstrated improvement in disease-free survival in the setting of postmastectomy patients. There is no trial that demonstrates benefit in the post lumpectomy LRR setting.

Chemotherapy Treatment	Rating	Comments
Trastuzumab	1	
Simple mastectomy (SM)	8	
SM + sentinel lymph node biopsy (SLNB)	1	This procedure is appropriate if the patient had prior SLND.
SM + LND or modified radical mastectomy	2	
Lumpectomy	3	This procedure is appropriate only in a clinical trial.
Quadrantectomy	3	This procedure is appropriate only in a clinical trial.
Lumpectomy + RT	3	This procedure is appropriate only in a clinical trial.
RT Volumes		
Whole breast +/- boost	1	
Partial breast RT	3	
Chest wall (after mastectomy)	1	
Supraclavicular (adequate LND)	1	
<u>Rating Scale:</u> 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 2: 42-year-old woman, 3.0-cm LRR in breast 6 years after BCT + chemotherapy for T1cN0 lesion. Biopsy showed invasive ductal carcinoma. ER/PR (-). HER-2 negative/nonamplified. EOD workup positive: liver and multiple bone metastases.

Treatment	Rating	Comments
Principles of Treatment		
Chemotherapy	9	
Simple mastectomy (SM)	2	
SM + LND or modified radical mastectomy	2	
Lumpectomy	2	For this procedure, consider a clinical trial.
Quadrantectomy	2	For this procedure, consider a clinical trial.
Lumpectomy + RT	2	For this procedure, consider a clinical trial.
Hormone therapy	1	

RT Volumes Treatment	Rating	Comments
Whole breast +/- boost	2	
Partial breast RT	1	
Chest wall (after mastectomy)	2	
Supraclavicular (adequate LND)	2	
<u>Rating Scale:</u> 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 3: 55-year-old woman, 1.5-cm LRR in breast 7 years after BCT with lumpectomy only + RT for original diagnosis of DCIS, not otherwise specified. Biopsy: invasive ductal carcinoma. ER/PR (-). HER-2 normal. EOD workup negative.

Treatment	Rating	Comments
Principles of Treatment		
Chemotherapy	8	
SM + LND or modified radical mastectomy	8	
SM + sentinel lymph node biopsy (SNLB)	8	
Simple mastectomy (SM)	2	
Lumpectomy	2	For this procedure, consider a clinical trial.
Quadrantectomy	2	For this procedure, consider a clinical trial.
Lumpectomy + RT	2	For this procedure, consider a clinical trial.
Hormone therapy	2	
RT Volumes		
Whole breast +/- boost	2	
Partial breast RT	2	
Chest wall (after mastectomy)	2	
Supraclavicular (adequate LND)	2	
<u>Rating Scale:</u> 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 4: 55-year-old woman, 7 nodules (1-2 cm in diameter) along MRM scar 3 years after MRM + chemotherapy + adjuvant chest wall/SCL

RT (50 Gy). Primary and LRR both ER/PR (–), HER-2 normal.

Treatment	Rating	Comments
Complete excision of recurrence	8	Perform this procedure if technically possible with primary closure with or without simple advancement flap.
Chemotherapy	7	This treatment can be considered for study.
Radiation therapy	7	For this treatment, use judgment on RT volume.
Hormone therapy	1	
<u>Rating Scale:</u> 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 5: 60-year-old woman, 2-cm nodule on MRM scar 4 years after MRM + chemotherapy without hormonal therapy for T1N1 [3 lymph nodes (LN) (+)]. Fine-needle aspiration (+). Primary ER/PR (+). Biopsy nodule ER/PR (+) by immunohistochemistry and HER-2 3+. Asymptomatic EOD workup negative.

Treatment	Rating	Comments
Principles of Treatment		
Complete excision of recurrence	8	
Radiation therapy	8	
Hormone therapy	8	
Chemotherapy	5	If patient recurred while on an aromatase inhibitor, consider a taxane with trastuzumab.
Trastuzumab	6	No clear data exists to support Herceptin but, given risk of distant disease, it could be considered.
RT Volumes		
Chest wall	9	
Supraclavicular fossa	8	
Axilla	2	
Internal mammary nodes (IMN)	2	
<u>Rating Scale:</u> 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 6: 65-year-old woman, 2-cm isolated axillary nodal recurrence detected on PE, confirmed on CT. Initial treatment MRM, chemotherapy, no adjuvant RT for T2N1M0 invasive ductal carcinoma, grade 2. LN biopsy (+), invasive ductal carcinoma, ER/PR (+), HER-2 nonamplified. Metastatic workup negative for distant metastases.

Treatment	Rating	Comments
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Principles of Treatment	Rating	Comments
Complete excision of recurrence	9	This procedure is appropriate if disease is surgically resectable without significant morbidity.
Radiation therapy	9	
Hormone therapy	9	
Chemotherapy	5	This treatment has no role in ER + disease. Limited data exist on the benefit in ER (–) disease; recent study shows benefit to chemotherapy at the time of recurrence.
Trastuzumab	1	
RT Volumes		
Chest wall	8	
Supraclavicular fossa	9	
Axilla	8	For this treatment, the field extent is dependent on surgical extent, i.e., axillary dissection versus excision of solitary LN.
Internal mammary nodes (IMN)	5	Strong consideration should be given if IMN are clinically or radiographically involved. Physicians must weigh 0%–2% subsequent recurrence rate in uninvolved IMN when not treated electively versus potential for morbidity from IMN irradiation.
<u>Rating Scale:</u> 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Summary of Literature Review

Introduction

For most of the recent decades, the major focus of radiation oncology in the management of breast cancer has been on performing both randomized and nonrandomized trials comparing breast-conserving therapy (BCT) using surgery and radiation with the more traditional modified radical mastectomy (MRM). With data confirming equivalent survival with these 2 local-regional therapies in the management of early-stage breast cancer, attention was then refocused on identifying factors (pathologic, patient, or therapy-oriented) that predicted the success or failure of the local-regional treatment.

Twenty-year rates of local-regional recurrence (LRR) in the intact breast after BCT have been reported to be 8.8%. Similarly low long-term crude recurrence rates (13%) for BCT were reported in the Danish trial as compared with mastectomy (21%). The relationship of local recurrence to the development of distant failure and death from disease is being well-studied. In early studies, the survival rate with salvage surgery for failures after BCT was 50% or higher at 5 years. These local recurrences were thought less likely to result in subsequent distant disease from local-regional failures when following BCT versus mastectomy, which were readily linked with the development of distant disease and death.

Today, any discussion about LRR treatment must be considered in the context of advances of systemic chemotherapy, hormonal therapy, and targeted agents such as trastuzumab in the management of breast cancer with patterns of survival and disease-free survival having changed. Women who decades ago would have died rapidly from distant disease may now exhibit a local-regional failure due to prolonged survival. Outcomes of these LRR failures without distant disease have been re-examined. Analysis of 2 prospective randomized trials from the European Organization for Research and Treatment of Cancer (EORTC) and the Danish Breast Cancer Group comparing mastectomy with BCT in patients of similar stages with similar systemic therapy showed almost identical 5-year actuarial local-regional and survival rates following salvage

procedures for early local-only failures in both the breast-conserved arm and the mastectomy arm. Thus, the relationship between local failure and distant failure must be reanalyzed in both patients treated with mastectomy as well as those treated with BCT.

As the radiation oncology field of breast cancer therapy continues to advance with the examination of alternate fractionation schema and methods such as hypofractionation and accelerated partial breast irradiation (APBI), obtaining local control with initial treatment must remain important, not only to prevent either the loss of the breast in the conserved patients or painful and difficult-to-control local failure in the mastectomy patients, but also to potentially decrease subsequent distant metastases that may be associated with these local failures. Data from the Early Breast Cancer Trialists Collaborative Group (EBCTCG) demonstrate that treatments resulting in improved local control may lead to decrease in breast cancer mortality. The overview analysis also suggests that avoidance of local recurrence after breast-conserving surgery (BCS) and radiation, and avoidance of local recurrence elsewhere after mastectomy, such as in the chest wall or regional nodes, are of comparable relevance to 15-year breast cancer mortality. As systemic therapeutic regimens become more effective in reducing the risk of distant disease, the goal of ensuring local-regional control takes on a potentially greater importance.

Randomized trial updates demonstrated the value of postmastectomy radiation therapy (PMRT) in stage II disease with 1 to 3 positive lymph nodes. The Danish Cooperative Breast Cancer Group 82b and 82C trials and the Vancouver British Columbia trial evaluated the local control and survival in mastectomy patients with 1 to 3 positive lymph nodes treated with systemic chemotherapy with or without PMRT. Radiation led to both decreased LRR and improved survival. Additional analysis of patients in the Danish trial who underwent a more complete axillary dissection of 8 or more removed lymph nodes also revealed both a significantly lower risk of 15-year LRR and improvement in survival in patients receiving radiation. Likewise, the value of regional nodal irradiation was demonstrated in the results from the MA 20 study in patients undergoing BCT.

Recurrence after Breast-conserving Surgery and Radiation

Predictors for local-regional failure after both BCS and radiation can be divided into 3 broad categories: patient, tumor, and therapeutic factor. Young age at the time of diagnosis (patients in their 30s and 40s), appears to be a strong predictor.

Several studies have found that positive microscopic margins, gross multifocality, and an extensive intraductal component are associated with a higher risk of recurrence in the conserved breast. Additionally, larger tumor size and lymphatic vessel invasion have been reported as risk factors for ipsilateral breast tumor recurrence (IBTR). Newer studies suggest that the molecular subtype may also impact local recurrence, with both triple negative (ER- [estrogen receptor], PR- [progesterone receptor] and HER [human epidermal growth factor receptor]-2-neu-) and HER-2-enriched (HER-2+) subtypes associated with a higher rate of local and regional relapse.

The third category of risk factors for IBTR consists of therapeutic factors, most importantly the omission of breast radiation. Numerous studies have demonstrated that radiation therapy (RT) significantly reduces the risk of recurrence in the breast. Patients receiving systemic chemotherapy or hormone therapy appear to have higher local control rates, all else being equal, than those who do not. The addition of a radiation boost to the lumpectomy cavity may decrease the incidence of a recurrence in the conserved breast, particularly in women younger than 40.

An increasing number of women are treated with APBI with either interstitial or balloon brachytherapy or external beam treatment. A limited long-term follow-up study regarding pattern of failure in breast or nodal regions is generally lacking. However, existing data do suggest that the rate of IBTR is comparable to whole-breast irradiation (WBI), with 10-year recurrence rates reported to be up to 6%. An update of the American Society of Breast Surgeons MammoSite brachytherapy trial evaluated patients treated with balloon brachytherapy APBI. With a median of 53.5 months of follow-up, the 5-year actuarial IBTR rates were 2.59%, 5.43%, and 5.28%, respectively for "suitable," "cautionary," and "unsuitable" as defined by the American Society of Radiation Oncology (ASTRO) consensus panel on APBI (P=.1884). The only factor on univariate analysis associated with the development of an IBTR was receptor-negative disease. A matched pair analysis of 199 patients receiving interstitial APBI versus WBI showed no differences in 12-year rates of local recurrences (3.8% versus 5%), regional recurrences (0% versus 1.1%), or cause-specific survival (78% versus 71%).

Neoadjuvant therapy is increasingly used in breast cancer patients in whom it is known that systemic therapy will be needed in an adjuvant setting or to increase chances of success with BCS. Data suggest that BCT can be used after neoadjuvant therapy with acceptable local control. In the NeOAdjuvant Herceptin trial of 235 patients with HER-2 positive locally advanced or inflammatory breast cancer were randomized to treatment with neoadjuvant trastuzumab plus chemotherapy or chemotherapy alone. Only 6 of 235 patients (2.5%) experienced either an IBTR or chest wall relapse with a median follow-up time of 3.2 years with the rate being similar in both BCT and mastectomy groups. None of the 4 patients undergoing BCT after chemotherapy with trastuzumab experienced an IBTR.

Following an IBTR in patients undergoing BCT, the 5-year survival rate is 76.6% for node-negative patients and 59.9% for node-positive patients. The generally recommended treatment for locally recurrent breast cancer after BCT using WBI is salvage mastectomy, although a repeat attempt at breast conservation may also be possible in select cases. The phase II trial 1014 is currently ongoing to evaluate repeat BCS followed by 3-D conformal partial breast reirradiation (see Variant 1, above.)

Limited data exist on salvage of patients who develop IBTR after APBI. Repeat BCS or mastectomy has been shown to produce excellent salvage rates comparable to the low rate of failures after WBI, but patient numbers are small. The rate of IBTR at 5 years was shown to be 3.6% for invasive breast cancer and 3.3% for DCIS out of 1,440 patients treated with balloon brachytherapy APBI. The 3-year disease-free survival and overall survival rate of 58% and 80%, respectively, after salvage mastectomy or repeat breast conservation. In this trial, 74% underwent salvage mastectomy, and 26% received BCT.

The incidence of any nodal recurrence in breast-conserving series is low. However, involvement of the nodes has significant impact on outcome; therefore, assessment of the axillary status for an invasive local recurrence of the breast should be considered. The role of sentinel lymph node biopsy (SLNB) in this scenario remains to be defined. Preliminary data indicate that SLNB may be performed at the time of salvage surgery, as previous breast conservation or axillary surgery may not be a contraindication to SLNB. Because of the relationship between local recurrence and distant failure, systemic therapy must also be considered in the treatment program for this patient group (see Variant 2, above.)

To date, no published series has shown a statistically significant improvement in subsequent outcome with the administration of salvage chemotherapy or hormonal intervention at the time of local recurrence. Factors to be considered in this clinical decision include 1) prior systemic therapy, if any; 2) extent of recurrence; 3) time from initial treatment to recurrence; 4) tumor hormone receptor status; 5) patient age; 6) tumor size; 7) margin status; and 8) general medical condition.

The National Surgical Adjuvant Breast and Bowel Project (NSABP) is evaluating the benefit of adjuvant chemotherapy following radical resection of recurrent LRR breast cancer. This prospective randomized trial is currently open to accrual.

Some patients who present with an IBTR following BCT may have a new primary tumor as opposed to a true local recurrence. The IBTR tumor is defined as a new primary if it is distinctly different from the original tumor with respect to histology subtype, if it presents in a different location in the breast, or if it is of different clonality. The time between the original primary and the second tumor is generally considerably greater for new primaries compared to true recurrences (average 55 months versus 33 months). In patients receiving RT as part of BCT, 10-year overall survival rates (75% versus 55%) and distant disease-free survival rates (85% versus 41%) tend to be much better for patients with new primaries compared to those with true recurrences. Thus, the diagnosis of a new primary as opposed to a true recurrence implies a different natural history and prognosis and has different implications for therapeutic management. Unfortunately, most series addressing breast tumor recurrences do not adequately distinguish between the 2 entities. This may be of particular importance to breast cancer management in young women with BRCA 1/2 gene mutations, who are at increased risk for breast tumor recurrences due to new primaries.

Patients with ductal carcinoma in situ (DCIS) who undergo BCT and subsequently sustain a recurrence in the treated breast appear to have an excellent outcome following salvage therapy. In most series, about half of the recurrences are invasive, with the other half recurring as DCIS. Nevertheless, almost all of these patients can be cured by mastectomy.

Analysis of outcomes of IBTR after breast conservation in NSABP B-17 and B-24 trials demonstrated that the 15-year cumulative incidence of invasive IBTR in patients treated with BCS was 19% with lumpectomy alone and 8.9% with lumpectomy and RT in B-17. In B-24, the 15-year cumulative incidence of invasive IBTR in patients treated with lumpectomy alone was 10% in lumpectomy and RT versus 8.5% with lumpectomy and tamoxifen. For noninvasive DCIS, the incidence of IBTR was 15.7% for lumpectomy only and 8.8% for lumpectomy and RT in B-17. In B-24, the incidence of IBTR for lumpectomy and RT was 8.3% and 7.5% with lumpectomy and tamoxifen. The probability of cancer-related death was 10.4% at 10 years after an invasive recurrence versus 2.7% after a noninvasive (DCIS) IBTR (see Variant 3, above.)

Recurrence after Mastectomy

Risk factors for local-regional failure following mastectomy can also be divided into clinical, pathological, and treatment-related categories. Young age (<35 years), nodal status, hormone receptor status, tumor size, lymphovascular invasion, multicentricity, and adequacy of nodal dissection as measured by the number of removed lymph nodes are all risk factors for postmastectomy recurrence. Elective PMRT reduces this risk. There is controversy regarding the risk of chest wall recurrence in the subgroup of patients with 1 to 3 positive nodes and their need for PMRT due to an unclear impact on survival and potential increased toxicity despite increased local control (see the National Guideline Clearinghouse [NGC] summary [Appropriateness Criteria® postmastectomy radiotherapy](#)).

Systemic therapy appears to have an impact on local-regional control. In the most recent meta-analysis of systemic therapy from the EBCTG, 5 years of tamoxifen therapy reduced the local recurrence rate by about one-half in women with hormone receptor-positive disease (local recurrence ratio of 0.47), whereas, irrespective of hormone receptor status, polychemotherapy reduced it by about one-third (ratios 0.63–0.70 depending on patient age).

Five-year survival rates range from 35% to 75%, and 10-year survival rates range from 25% to 55% after LRR. Long-term control of the local-regional disease is achieved in only 45% to 70% of patients. Most patients with early LRR develop distant metastases, but a favorable subgroup exists with a lower risk of distant metastases and improved 5- and 10-year survival rates. Prognostic factors include the extent of disease (EOD)

initially and at recurrence, the disease-free interval, grade, and the ER status as well as the use of surgical excision, radiation, and hormonal therapy. Patients with uncontrolled local-regional disease are usually symptomatic, are more likely to develop distant metastases, and die sooner than patients who have controlled LRR. Consequently aggressive attempts at controlling the LRR are warranted.

A multidisciplinary approach is required for the management of a chest wall recurrence after mastectomy (see Variants 4 and 5, above).

Surgical resection should be performed if the size and location of the recurrence permit. In patients who have not received prior RT, LRRs are managed with irradiation. LRR after mastectomy is a harbinger of distant metastases, so systemic treatment should also be considered. If the patient is ER-positive, then tamoxifen, an aromatase inhibitor (depending on menopausal status), or ovarian ablation may be used. If the patient is ER-negative, then chemotherapy may be given. Although it is a reasonable treatment, chemotherapy has not historically been proven to impact overall survival after a recurrence. It has not been well studied. However, data from the CALOR trial presented at 2012 at the San Antonio Breast Cancer Symposium show a benefit to chemotherapy, predominantly in ER-negative women.

Treatment Guidelines after Breast-conserving Therapy

For patients failing BCT that included standard WBI and an axillary node dissection, simple mastectomy is recommended as the local treatment of choice when the failure is confined to the breast parenchyma and is operable. The role of partial breast irradiation in this setting is currently under investigation, and consideration should be given to placing the patient on an available clinical trial. The Radiation Therapy Oncology Group® (RTOG®) phase II trial 1014 is currently open for accrual. It uses 3-D conformal partial breast irradiation for patients with an in-breast local recurrence ≤ 3 cm and 3 or more positive lymph nodes without extranodal extension.

In the clinical situation involving recurrence in the treated breast, along with a supraclavicular nodal failure, radiation to the untreated supraclavicular area plus chemotherapy is the recommendation. Although this pattern of recurrence is not common, it is viewed as systemic failure based on existing evidence. Similarly, for patients with clear distant metastases as well as local failure, primary systemic management is recommended rather than mastectomy.

In the rare clinical situation of a local recurrence for a patient whose initial treatment consisted only of a wide local excision without radiation or axillary dissection, treatment options include simple excision or lumpectomy, axillary nodal evaluation, and RT in the absence of distant metastasis.

Given the situation of a patient with recurrent DCIS treated initially with lumpectomy plus RT only, simple excision is recommended.

Treatment Guidelines for Local Recurrence after Mastectomy

Treatment options for LRR following mastectomy include surgery, RT, chemotherapy, hormonal therapy, or a combination of modalities. Patients experiencing LRR after mastectomy should undergo a workup for metastatic disease. In the absence of distant metastases, aggressive attempts at salvage should be entertained. When possible, surgical excision followed by RT to the involved chest wall and regional lymphatics is the standard treatment approach. One study reported an overall survival after chest wall recurrence of 46% at 5 years and 28% at 10 years for patients treated with full-course external beam irradiation. Ten-year local-regional disease control was achieved in 79% of patients, with a distant metastasis-free survival rate of 49% at 5 years and 40% at 10 years. In this series, HER-2 status was the only significant factor affecting local-regional progression. Patients with HER-2 positive disease had a local-regional progression-free rate of 59% compared with 92% for patients with HER-2 negative disease. Both PR-positive status and time longer than 2 years from the original diagnosis to chest wall recurrence were associated with favorable distant metastasis-free and long-term survival. Along with disease-free interval, the adequacy of local control for LRR has also been shown to have a favorable impact on long-term survival.

Isolated Axillary and Supraclavicular Nodal Failures

Isolated nodal recurrences in the axillary or supraclavicular nodal regions occur less frequently than chest wall or in-breast recurrences. In a review of 1,614 breast cancer patients undergoing either lumpectomy or mastectomy, only 14 patients (0.9%) developed an ipsilateral nodal recurrence after axillary dissection. Isolated supraclavicular recurrence is similarly uncommon.

If feasible, surgery is usually used as the initial treatment modality. Radiation therapy is generally used after surgery if the patient has not seen prior radiation. Systemic therapy may also be incorporated in the salvage therapy although the role of systemic therapy in this setting is unclear. Surgery, however, may not be technically feasible due to prior axillary dissection. Likewise, supraclavicular disease may not be amenable to surgical resection due to potential postoperative morbidity. In addition, patients who have received prior axillary or supraclavicular RT are usually not candidates for reirradiation. Both isolated axillary and supraclavicular relapses are generally associated with a poor long-term survival due to high rate of subsequent distant metastasis. However, subsets of patients with favorable features including a single axillary nodal recurrence, greater than 1-year disease free interval, attainment of local control have been identified with 10 year survivals reported at 69%. In the absence of distant metastasis, aggressive attempts at salvage should be entertained (see Variant 6, above).

Summary

- Five-year actuarial LRR and survival rates following salvage procedures for early local-only failures are similar in patients undergoing mastectomy versus BCT.
- Salvage mastectomy is generally recommended for locally recurrent breast cancer after BCS. Repeat attempts at breast conservation may be considered, preferably through participation in a clinical trial.
- To date, no published series has shown statistically significant improvement in outcome with salvage chemotherapy or hormonal therapy in the case of local recurrence after BCT.
- Multidisciplinary management of chest wall recurrence after mastectomy is warranted, including surgery, RT, and systemic therapy. In the absence of distant metastasis, aggressive attempts at salvage should be entertained.
- Multidisciplinary management of isolated axillary or supraclavicular nodal recurrence is warranted where feasible with surgery and RT, although risk of systemic failure is high. The benefit of systemic therapy in this setting remains to be determined.

Abbreviations

- BCT, breast-conserving therapy
- CT, computed tomography
- DCIS, ductal carcinoma in situ
- EOD, extent of disease
- ER, estrogen receptor
- HER, human epidermal growth factor receptor
- LN, lymph node
- LND, lymph node dissection
- LRR, local-regional recurrence
- MRM, modified radical mastectomy
- PE, physical examination
- PR, progesterone receptor
- RT, radiation therapy
- SAKK, Swiss Group for Clinical Cancer Research
- SCL, supraclavicular
- SLNB, sentinel lymph node biopsy
- SLND, sentinel lymph node dissection
- SM, simple mastectomy

Clinical Algorithm(s)

Algorithms were not developed from criteria guidelines.

Scope

Disease/Condition(s)

Breast cancer

- Local-regional recurrence (LRR) after breast-conserving therapy (BCT)
- LRR after modified radical mastectomy (MRM)

Guideline Category

Management

Risk Assessment

Treatment

Clinical Specialty

Obstetrics and Gynecology

Oncology

Radiation Oncology

Radiology

Surgery

Intended Users

Health Plans

Hospitals

Managed Care Organizations

Physicians

Utilization Management

Guideline Objective(s)

To evaluate the appropriateness of radiation, chemotherapy, surgery, and hormonal treatment procedures for patients with local-regional recurrence (LRR) of breast cancer after breast-conserving therapy (BCT) or modified radical mastectomy (MRM)

Target Population

Women with local-regional recurrence (LRR) of breast cancer after breast-conserving therapy (BCT) or modified radical mastectomy (MRM)

Interventions and Practices Considered

1. Chemotherapy
2. Simple mastectomy (SM)
 - Alone
 - Plus sentinel lymph node biopsy (SNLB)
 - Plus lymph node dissection (LND) or modified radical mastectomy (MRM)
3. Lumpectomy
 - Alone
 - Plus radiation therapy (RT)
4. Quadrantectomy
5. Hormone therapy
6. Complete excision of recurrence
7. RT including consideration of radiation volumes
8. Trastuzumab

Major Outcomes Considered

- Overall and disease-free survival rates

- Recurrence rates

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Literature Search Procedure

Staff will search in PubMed only for peer reviewed medical literature for routine searches. Any article or guideline may be used by the author in the narrative but those materials may have been identified outside of the routine literature search process.

The Medline literature search is based on keywords provided by the topic author. The two general classes of keywords are those related to the condition (e.g., ankle pain, fever) and those that describe the diagnostic or therapeutic intervention of interest (e.g., mammography, MRI).

The search terms and parameters are manipulated to produce the most relevant, current evidence to address the American College of Radiology Appropriateness Criteria (ACR AC) topic being reviewed or developed. Combining the clinical conditions and diagnostic modalities or therapeutic procedures narrows the search to be relevant to the topic. Exploding the term "diagnostic imaging" captures relevant results for diagnostic topics.

The following criteria/limits are used in the searches.

1. Articles that have abstracts available and are concerned with humans.
2. Restrict the search to the year prior to the last topic update or in some cases the author of the topic may specify which year range to use in the search. For new topics, the year range is restricted to the last 10 years unless the topic author provides other instructions.
3. May restrict the search to Adults only or Pediatrics only.
4. Articles consisting of only summaries or case reports are often excluded from final results.

The search strategy may be revised to improve the output as needed.

Number of Source Documents

The total number of source documents identified as the result of the literature search is not known.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Strength of Evidence Key

Category 1 - The conclusions of the study are valid and strongly supported by study design, analysis and results.

Category 2 - The conclusions of the study are likely valid, but study design does not permit certainty.

Category 3 - The conclusions of the study may be valid but the evidence supporting the conclusions is inconclusive or equivocal.

Category 4 - The conclusions of the study may not be valid because the evidence may not be reliable given the study design or analysis.

Methods Used to Analyze the Evidence

Description of the Methods Used to Analyze the Evidence

The topic author drafts or revises the narrative text summarizing the evidence found in the literature. American College of Radiology (ACR) staff draft an evidence table based on the analysis of the selected literature. These tables rate the strength of the evidence (study quality) for each article included in the narrative text.

The expert panel reviews the narrative text, evidence table, and the supporting literature for each of the topic-variant combinations and assigns an appropriateness rating for each procedure listed in the table. Each individual panel member assigns a rating based on his/her interpretation of the available evidence.

More information about the evidence table development process can be found in the ACR Appropriateness Criteria® Evidence Table Development document (see the "Availability of Companion Documents" field).

Methods Used to Formulate the Recommendations

Expert Consensus (Delphi)

Description of Methods Used to Formulate the Recommendations

Rating Appropriateness

The appropriateness ratings for each of the procedures included in the Appropriateness Criteria topics are determined using a modified Delphi methodology. A series of surveys are conducted to elicit each panelist's expert interpretation of the evidence, based on the available data, regarding the appropriateness of an imaging or therapeutic procedure for a specific clinical scenario. American College of Radiology (ACR) staff distribute surveys to the panelists along with the evidence table and narrative. Each panelist interprets the available evidence and rates each procedure. The surveys are completed by panelists without consulting other panelists. The appropriateness rating scale is an ordinal scale that uses integers from 1 to 9 grouped into three categories: 1, 2, or 3 are in the category "usually not appropriate"; 4, 5, or 6 are in the category "may be appropriate"; and 7, 8, or 9 are in the category "usually appropriate." Each panel member assigns one rating for each procedure for a clinical scenario. The ratings assigned by each panel member are presented in a table displaying the frequency distribution of the ratings without identifying which members provided any particular rating.

If consensus is reached, the median rating is assigned as the panel's final recommendation/rating. Consensus is defined as eighty percent (80%) agreement within a rating category. A maximum of three rounds may be conducted to reach consensus. Consensus among the panel members must be achieved to determine the final rating for each procedure.

If consensus is not reached, the panel is convened by conference call. The strengths and weaknesses of each imaging procedure that has not reached consensus are discussed and a final rating is proposed. If the panelists on the call agree, the rating is proposed as the panel's consensus. The document is circulated to all the panelists to make the final determination. If consensus cannot be reached on the call or when the document is circulated, "No consensus" appears in the rating column and the reasons for this decision are added to the comment sections.

This modified Delphi method enables each panelist to express individual interpretations of the evidence and his or her expert opinion without excessive influence from fellow panelists in a simple, standardized and economical process. A more detailed explanation of the complete process can be found in additional methodology documents found on the [ACR Web site](#) (see also the "Availability of Companion Documents" field).

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

Criteria developed by the Expert Panels are reviewed by the American College of Radiology (ACR) Committee on Appropriateness Criteria.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The recommendations are based on analysis of the current literature and expert panel consensus.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Selection of appropriate radiation therapy, surgery, chemotherapy, and hormonal therapy for management of patients with local-regional recurrence of breast cancer

Potential Harms

Not stated

Qualifying Statements

Qualifying Statements

The American College of Radiology (ACR) Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists, and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the U.S. Food and Drug Administration (FDA) have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

Halyard MY, Haffty BG, Harris EE, Bailey L, Bellon JR, Freedman GM, Goyal S, Horst KC, Moran MS, Park CC, Suh WW, Toppmeyer D, Expert Panel on Radiation Oncology—Breast. ACR Appropriateness Criteria® local-regional recurrence (LRR) and salvage surgery--breast cancer. [online publication]. Reston (VA): American College of Radiology (ACR); 2013. 12 p. [51 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

1996 (revised 2013)

Guideline Developer(s)

American College of Radiology - Medical Specialty Society

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The American College of Radiology (ACR) provided the funding and the resources for these ACR Appropriateness Criteria®.

Guideline Committee

Committee on Appropriateness Criteria, Expert Panel on Radiation Oncology—Breast

Composition of Group That Authored the Guideline

Panel Members: Michele Y. Halyard, MD (*Principal Author*); Bruce G. Haffty, MD (*Panel Chair*); Eleanor E. R. Harris, MD (*Panel Vice-chair*); Lisa Bailey, MD; Jennifer R. Bellon, MD; Gary M. Freedman, MD; Sharad Goyal, MD; Kathleen C. Horst, MD; Meena S. Moran, MD; Catherine C. Park, MD; W. Warren Suh, MD; Deborah Toppmeyer, MD

Financial Disclosures/Conflicts of Interest

Not stated

Guideline Status

This is the current release of the guideline.

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Guideline Availability

Electronic copies: Available from the [American College of Radiology \(ACR\) Web site](#) .

Print copies: Available from the American College of Radiology, 1891 Preston White Drive, Reston, VA 20191. Telephone: (703) 648-8900.

Availability of Companion Documents

The following are available:

- ACR Appropriateness Criteria®. Overview. Reston (VA): American College of Radiology; 2013 Nov. 3 p. Electronic copies: Available in Portable Document Format (PDF) from the [American College of Radiology \(ACR\) Web site](#) .
- ACR Appropriateness Criteria®. Literature search process. Reston (VA): American College of Radiology; 2013 Apr. 1 p. Electronic copies: Available in PDF from the [ACR Web site](#) .
- ACR Appropriateness Criteria®. Evidence table development – diagnostic studies. Reston (VA): American College of Radiology; 2013 Nov. 3 p. Electronic copies: Available in PDF from the [ACR Web site](#) .
- ACR Appropriateness Criteria®. Evidence table development – therapeutic studies. Reston (VA): American College of Radiology; 2013 Nov. 4 p. Electronic copies: Available in PDF from the [ACR Web site](#) .
- ACR Appropriateness Criteria® local-regional recurrence (LRR) and salvage surgery—breast cancer. Evidence table. Reston (VA): American College of Radiology; 2013. 27 p. Electronic copies: Available from the [ACR Web site](#) .

Patient Resources

None available

NGC Status

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